

ORD Partners with DOE's Joint Genome Institute to Solve Computational Toxicology Problems

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Collaboration between EPA and DOE will produce DNA sequence data on organisms of special importance to EPA's effort to apply molecular data to the prediction of toxicity, characterization of exposure, and, ultimately, integration in ecological risk assessments. These are primary goals for ORD's new Computational Toxicology Initiative. The organisms include the fathead minnow (*Pimephales promelas*), the African clawed frog (*Xenopus laevis*), and the freshwater crustacean *Daphnia pulex*. The Department of Energy's Joint Genome Institute is expanding its mission to bring high-throughput DNA sequencing and bioinformatics expertise to the greater academic, government, and industrial scientific community. DOE is beginning its partnerships with EPA by collaborating on gene sequencing projects.

The fathead minnow (*P. promelas*) has been used for decades as a sentinel for aquatic ecological risk assessment and remains a standard model for aquatic toxicity testing. A fuller set of *Pimephales* gene sequences will allow government and industry to develop more tools for predicting toxicity in aquatic organisms and improving aquatic ecosystems monitoring. Such new tools will provide reliable science to support sound regulatory determinations and environmental decisions. EPA will collaborate with DOE on the development and sequencing of complementary DNA libraries from different tissues of unexposed fathead minnows at different developmental stages, as well as sequencing of libraries from tissues of minnows exposed to chemical stressors of particular programmatic importance. Gene sequencing of these libraries will yield thousands of gene fragment sequences that will aid in constructing the first large-scale DNA microarrays for research use.

X. laevis has long served as a model for the study of embryonic development and developmental toxicology. Biological processes in the frog provide a great deal of insight into human biological processes. EPA will join DOE and the international amphibian research community in work already in progress, the whole genome sequencing of *Xenopus tropicalis*, an organism closely related to *X. laevis*.

DOE's plans to sequence the genome for *D. pulex*, an invertebrate organism, will contribute unique data for EPA's ecological risk assessments and historical use of invertebrate toxicity tests. Mechanisms in invertebrates may relate well to that of aquatic vertebrates (e.g., fathead minnow) and thus support species extrapolation hypotheses (i.e., the current thinking that there may be valid comparisons between the biological mechanisms in invertebrates and invertebrates [including humans]). The sequencing is part of plans developed under an international Daphnia Genomics Consortium, which includes DOE and EPA molecular biologists.